

1/16

FIGURE 1

CCTTCCCTGCTGTAAAGATTCAACATTTTAAATCAGTTAAATACTTTGTCTCTCTGTCTCTCCATCAGAAAGTAAATACATAAGAA 30
 M H Y F G V L A A L S V F M I I A C L T R G K P L E N W K K
 ATGCATTATTTGGAGATTAGCTGCACCTGCTGTTTCAATATCATTTGCCTGCCTGCAAGAGGCCAAGCCTTTGGAAACTGGAAAG 60
 L P V M E E S D A F F H D P G E V E H D T H F D F K S F L E
 CTACCAGTTATGGAAGAGTCTGATGCCATTCCTTCATGATCCTGGGGAAGTGGAAACATGACACCCACTTTGACTTTAAATCTTTCTTGGAG 90
 N M K T D L L R S L N L S R V P S Q V K T K E E P P Q F M I
 AATATGAACACAGATTTACTAAGAAAGTCTGAATTTATCAAGGTCCCTCACAAGTGAAGACCAAGAAAGAGCCACACAGTTCATGATT 120
 D L Y N R Y T A D K S S I P A S N I V R S F S T E D V V S L
 GATTTATACACAGATATACAGGGGACAGTCCTCCATCCCTGCATCCACATCGTGAGGAGCTTCAGCACTGAAGATGTTGTTTCTTTA 150
 I S P E E H S F Q K H I L L F N I S I P R Y E E V T R A E L
 ATTTACCAGGAAGACACTCATTTCAGAAACACATCTTGCTCTTCAACATCTCTATTTCCACGATATGAGGAAGTCCACAGAGCTGAAC TG 180
 R I F I S C H K E V G S P S R L E G N M V I Y D V L D G D H
 AGAATCTTTATCTCCTGTCAAGGAAGTTGGTCTCCCTCCAGACTGGAAGCAACATGCTCATTTATGATGTTCTTAGATGGAGACCAT 210
 W E N K E S T K S L L V S H S I Q D C G W E M F E V S S A V
 TGGGAACACAAAGAAAGTACCAATCTTTACTTGTCTCTCACAGTATTCAGGACTGTGGCTGGGAGATGTTTGAGCTGTCCAGCGCTGTG 240
 K R W V K A D K M K T K N K L E V V I E S K D L S G F P C G
 AAAAGATGGGTCAAGGCAGACAAGATGAAGACTAAACAAAGCTAGAGTTGTTATAGAGAGTAAGGATCTGAGTGGTTTTTCTTCTGTGGG

2/16

FIGURE 1 (CONTINUED)

K L D I T V T H D T K N L P L L I V F S N D R S N G T K E T 270
 AAGCTGGATATTACTGTTACTCATGACACTAAAATCTGCCCTATTAAATAGTCTTCTCCAATGATCGCAGCAATGGGACAAAAGAGACC
 K V E L R E H I V H E Q E S V L N K L G K N D S S S E E E Q 300
 AAGTGGAGCTCGGCGAGATGATTGTTCAATGAACAGAAAGTGTGCTAAACAAATTAGGAAGAAGCGACTCTTCATCTGAAGAAGAACAG
 R E E K A I A R P R Q H S S R S K R S I G A N H C R R T S L 330
 AGAGAAGAAAAGCCATTGCTAGGCCCCGTCAGCATTCTCCAGAMGCAAGAGAGCATAGGACMAACCCTGTGCGAGAAAGTCACTC
 H V N F K E I G W D S W I I A P K D Y E A F E C K G G C F F 360
 CATGTGAACCTTTAAGAAATAGTTGGGATTCTTGGATCATTCGACCCCAAGATTATGAGGCTTTTGAGTGTAAAGGAGGTTGCTTCTTC
 P L T D N V T P T K H A I V Q T L V H L Q N P K K A S K A C 390
 CCCCTCACAGATAATGTTACGCCCAACCAACATGCTATTGTCCAGACTCTGGTGCACTCCAAAACCCMAAGAAAGCTTCCAAGGCCTGT
 C V P T K L D A I S I L Y K D D A G V P T L I Y N Y E G M K 420
 TGTGTTCCAACTAAATTGGATGCAATCTCTATTCTTTATAGGATGATGCTGGTGTGCCCACTTTTGATATATTAACCTATGAAGGGGATGAA
 V A E C G C R 427
 GTGGCAGAAATGTGCTGCAGTAGTATATGCTGAATATCTAAGAATATATACTTTTCTGCTGCTCTGTGAACTGTACATTAGTAGTGCAA
 ATGAAATCCTTGCAACACAGCTTTGGAGCACGGCATGGGCTGTTGTTGTTGCTGCTTTTAAAGGAAAGATGCGCATTTTAAAGAATGGC
 AATCACTGTAATACCTGCAATTATATACCATTAATTAAACTTTGTGAGATTGAAAAAATAAAAAAATAAAAAA

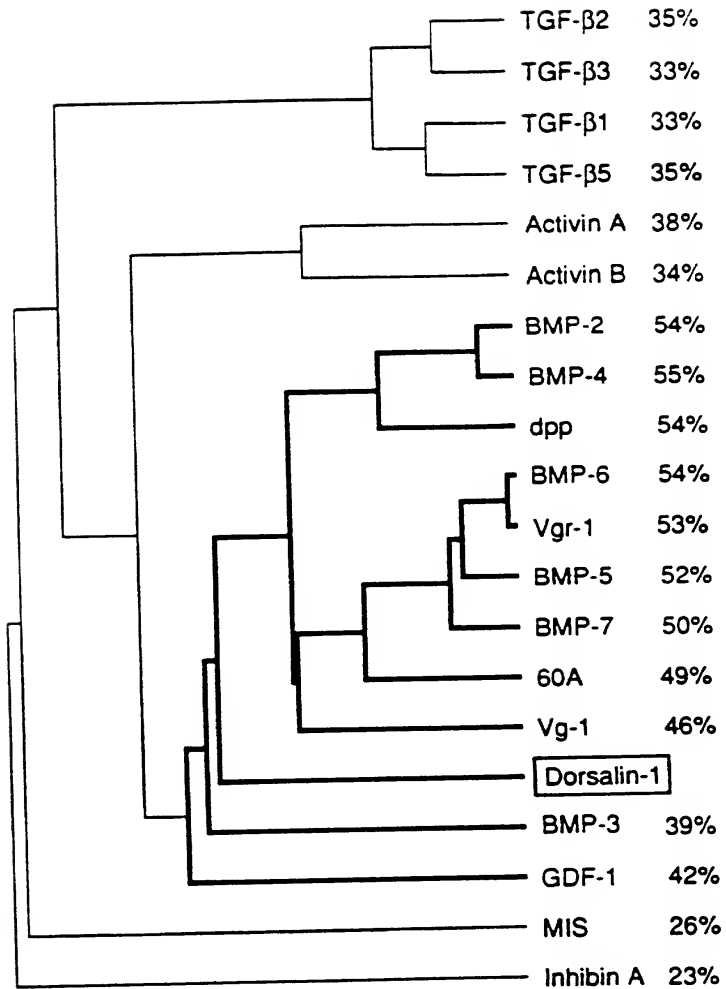
FIGURE 2A

```

DORSALIN-1 ..SVLNKLGKNDSSSEEEQREEKAIARPRQHSSRSKR^SIGANHGRRRTSLHVNF--KEIGMDSMIIAPKDYEAFECKGGGF
BMP-2 ..EHSWSQIRPLLVTFGHGKGHPHKKREKQAKHKQKALKSSCKRHPLYVDF--SDVGHNDVIIVAPPGYHAFYGHGEGCF
DPP ..DDGRHKARSIR^DVSGGEGGKGGRNKRHARRPTRRKNHDDTCRRHSLYVDF--SDVGHNDVIIVAPLGYDAYVGHGKCF
BMP-6 ..RTRR^SASSRRRQQRMRSTQSQDVARVSSASDYNSSSELKTACRKHELTVSEF--QDLGVQMDVIIAPKGYAANYCDGEGCS
VG-1 ..ECKDIQIFLYTSLLTVTLNPLRCKPRKRYSKLPFTASNICKKRHLTVSEF--KDVGVQMDVIIAPKGYAANYCYGEGCF
ACTIVA-A ..GADEEKEQSHRPFLMLQARQSEDPHPRRRR^GLECDGKVNICKKQFFVSEF--KDIGVNDVIIAPSGYHANYCEGEGCF
TGF-BETA-1 ..GMNRPFLLLMATPLERAQHLQSSRRRR^ALDTNYCFSSTEKNQCVRRQLYIDFRKDKLGUK-WIHEPKGIHANYCLGPGCF*
DORSALIN-1 FPLTDNVIPTKHAIVQTLVHLQ-----NPKKASKACCCVPTKLDATSLIYKDDAGVPTLIYNVEGMDKVAEGGCR [427]
BMP-2 FPLADHLNSTINHAIVQTLVNSV-----NLSKIPKACCVPTELSAISMLYLDENKVLK--NMDMVVEGGCCR [396]
DPP FPLADHFNSTINHAIVQTLVNNM-----NPKVPTACCVPTQLDSVAMLYLNDQSTVVLK--NVDQEMTVVCGGCR [588]
BMP-6 FPLNAHMAATINHAIVQTLVHLM-----NPEYVPKCCAPTKLNAISULYFDDNSNVIK--KVRNMTVVRACGCH [514]
VG-1 FPLNAHMAATINHAIVQTLVHSI-----EPEDPLPCGVPTKHSPLSMIFYDNDNDNVLR-HLENNMAYDECGGR [360]
ACTIVA-A SHIAGTSGSLSFHSTVINHYMRGHSPFANLSCCVPTKLRPHSALYDDGQNIKK--DIQNMIVVEECGCS [427]
TGF-BETA-1 -----YIMSLDIQISKVLALY-NQHNPAGASAA^CCVPQALEPLIVNY-VGRKPKVE--QLSNNIVRSCKGS [390]

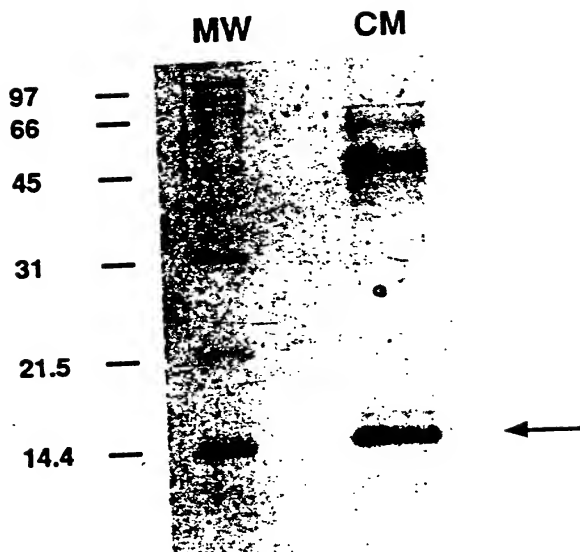
```

FIGURE 2B



5/16

FIGURE 3A



10002278-110201

6/16

FIGURE 3B

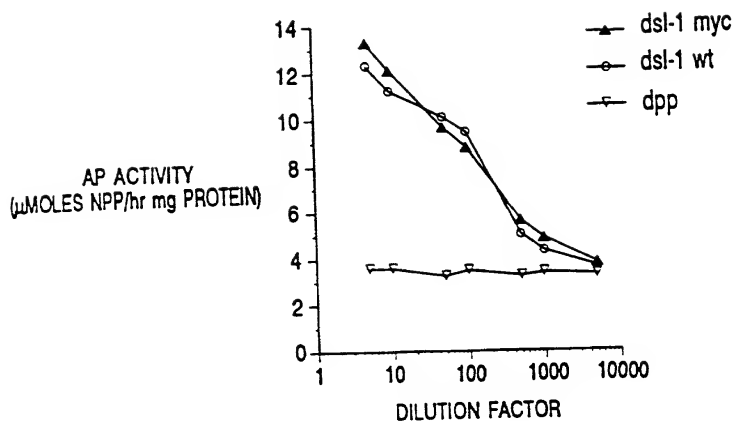


FIGURE 4A



FIGURE 4B

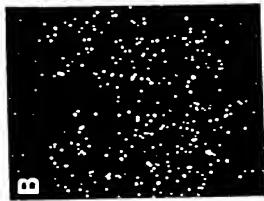


FIGURE 4C

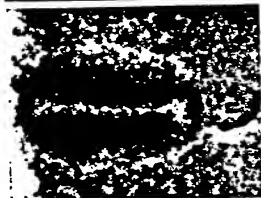


FIGURE 4D

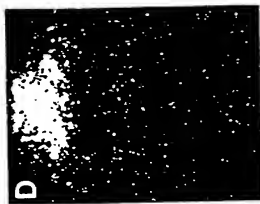


FIGURE 4E

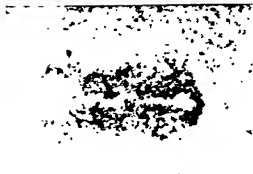


FIGURE 4F

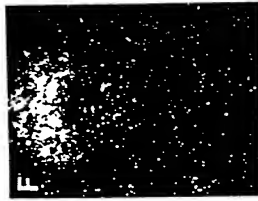


FIGURE 4G

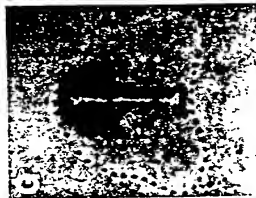
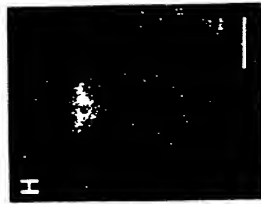


FIGURE 4H

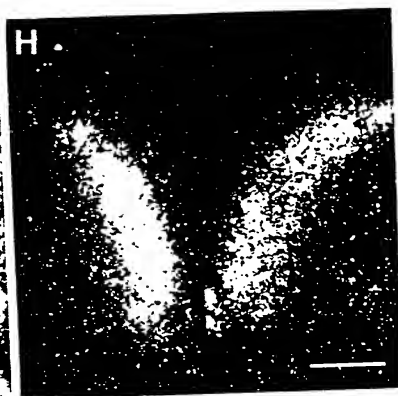


9/16

FIGURE 5G



FIGURE 5H



10002275.110201

FIGURE 6C



FIGURE 6B



FIGURE 6A

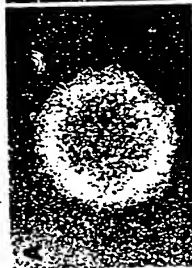


FIGURE 6F



FIGURE 6E



FIGURE 6D



11/16
FIGURE 6G

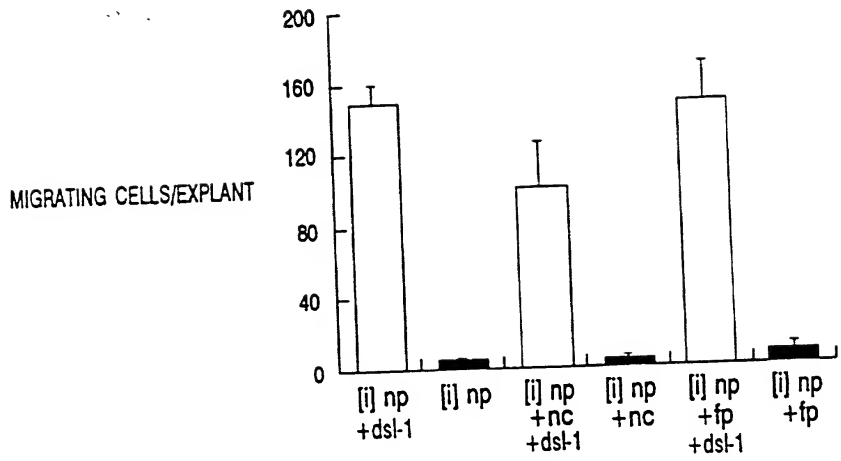


FIGURE 7A



FIGURE 7B



FIGURE 7C

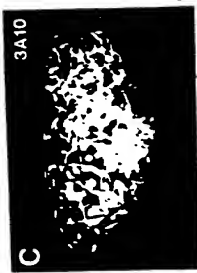


FIGURE 7D



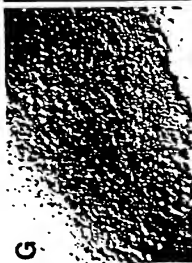
FIGURE 7E



FIGURE 7F



FIGURE 7G



G

FIGURE 7H



H

FIGURE 7I



I

FIGURE 7J



J

FIGURE 7K



K

FIGURE 7L



L

14/16
FIGURE 8A

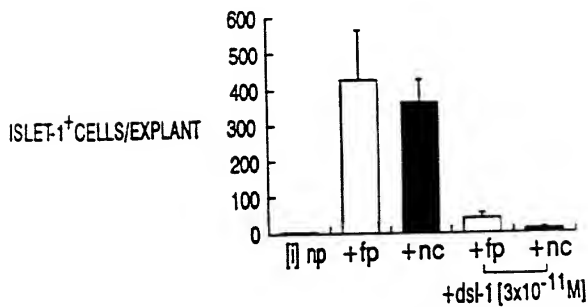


FIGURE 8B

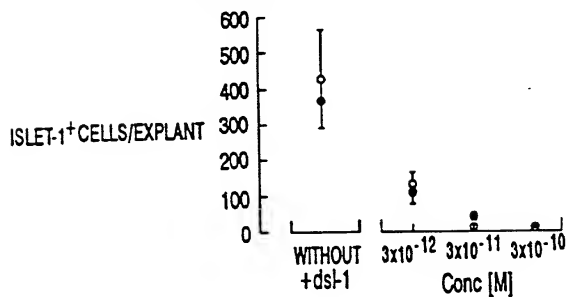


FIGURE 8C

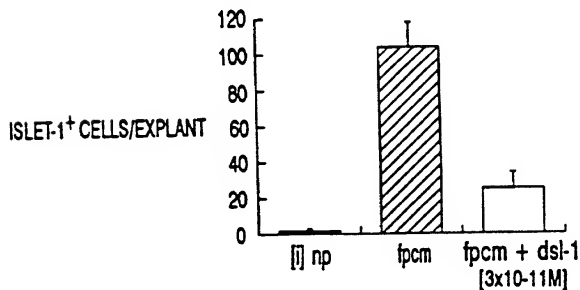
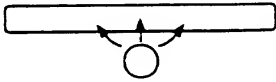


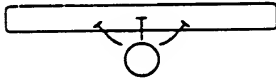
FIGURE 9A

A. ESTABLISHMENT OF DORSALIN-1 EXPRESSION

- i) SIGNALS FROM THE NOTOCHORD SPECIFY THE VENTRAL FATE OF OVERLYING NEURAL PLATE CELLS



- ii) SIGNALS FROM THE NOTOCHORD ACT ON OVERLYING NEURAL PLATE CELLS TO PREVENT SUBSEQUENT DSL-1 EXPRESSION



- iii) RESTRICTED DORSAL EXPRESSION OF DSL-1 OCCURS AFTER NEURAL TUBE CLOSURE

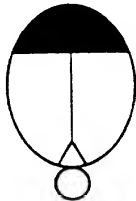
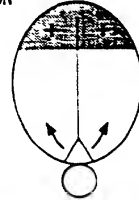


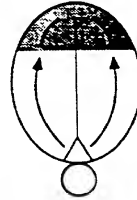
FIGURE 9B

B. POSSIBLE FUNCTIONS OF DORSALIN-1

- i) PROMOTION OF DORSAL CELL TYPE DIFFERENTIATION



- ii) LIMITING THE SPREAD OF VENTRAL SIGNALS



- iii) DIFFUSION OF DSL-1 CONTROLS CELL PATTERN MORE VENTRALLY

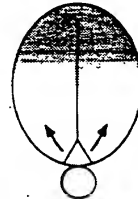


FIGURE 10

1	80	
B29	80	HHYFGVLAALSVEFNIIACLTRGKPLENWKKLPMVEESDAFFHDPCEVEHDTFDFKSFLENMKTDLRLSLNLSRVPSSQVK
B29m	
B29m	
B29	160	TKKEPPQMIDLYNRYTADKSSIPASNIVRSFSTEDVVSLISPEHSFQKHILLFNISIPRYEEVTRAEALRIFISCHKEV
B29m	
B29m	
B29	240	GSPSRLEGNMVIYDVL.DGOHWENKESTKSLLVSHSIQDCGWEMFEVSSAVKRWVKADKMKTNNKLEWIESKDLSGFPC
B29m		DVLEDSETHDQATGKTFLVSQDIRDEGMETLEEVSSAVKRWVRADSTTNKNKLEVTQVSHRES...C
B29m	
B29	320	GKLDITVTHDTKNLPLLI VFSNDRSNGTKETKVE.LREMIVHEQESVLNKLGNKNDSSSEEEQREEKAI...ARPRQHSSR
B29m		DTLDTISVPPGSKNLPLFFVVFVSNDRSNGTKETRLDLLKEMIGHEQETHLVKTKANNAYQAGESQEEGLDGYTAVGPLLAR
B29m	
B29	400	SKRSIGA.NHCRRSTSLHVNFKBIGWDSWIIAPKDYAEFECKGGCFPLTDNVTPTKHAIVQTLVHLQNPKKKSKACCCVPT
B29m		RKRSTGASSHCQKTSLRVNFEIDIGWDSWIIAPKEYDAYECKGGCFPLADDVTPTKHAIVQTLVHLKFPTKVGVKACCCVPT
B29m	
B29	433	KLDAISILYKDDAGVPTLIYNYEGMKVAECGCR
B29m		KLSPISILYKDDMGVPTLKYYHYEGHMSVAECGCR
B29m	